Computer-integrated patient-controlled epidural analgesia: a preliminary study on a novel approach of providing pain relief in labour

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ABSTRACT

Introduction: The need for individualisation of analgesic therapy in labour cannot be overemphasised. We have devised a programme, based on a novel clinical algorithm, that converts a continuous infusion pump into a patient-controlled epidural analgesia (PCEA) pump that is responsive to the patient's needs by varying its rate of infusion.

Methods: In this double-blinded, controlled trial, 40 American Society of Anesthesiologists I patients were recruited to receive either a continuous infusion of 10 ml/hour (Continuous Epidural Infusion [CEI], n=20) or the computer-integrated (CI) regimen (CI-PCEA, n=20) to maintain epidural analgesia after successful induction of combined spinal analgesia during early labour. The proportion of patients who had delivered without a requirement for analgesic supplementation was the primary outcome measure.

Results: There was a significant difference in the incidence of breakthrough pain, i.e. the primary outcome measure (two in CI-PCEA versus eight in the CEI group, p-value is 0.027). There was a trend towards a longer duration before analgesic supplementation of analgesia was required after its induction with CI-PCEA than CEI (p-value is 0.06). We could not detect a difference in the total hourly consumption of epidural analgesics between the two groups.

Conclusion: Our study also showed that with the CI-PCEA programme, we were able to convert an ordinary infusion pump to one which analyses the patients' needs in the previous hour (based on analgesic demands) and automatically adjusts the basal infusion accordingly. CI-PCEA reduced the incidence of breakthrough pain without the evidence of increasing drug consumption when compared with CEI.

Keywords: computer integration, labour analgesia, patient-controlled epidural analgesia

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INTRODUCTION

Neuraxial blocks have gained much popularity as a means of providing labour analgesia. In our institution, the use of a continuous infusion to maintain epidural analgesia has been the usual practice for the last ten years. A continuous infusion is issued to substitute the need for the anaesthetist to reinstate analgesia in the event of a breakthrough pain. However, the flexibility of customising analgesia is lacking. As well as according patients' autonomy in this respect, patient-controlled epidural analgesia (PCEA) has been shown to be very effective and desirable[1]. Despite that, the optimal regimen of PCEA has not been resolved – especially with regard to the role of a basal infusion. While the lack of a basal infusion has been shown to reduce analgesic consumption[2,3], the increased need for analgesic supplementation by the anaesthetist is still a subject of debate[4]. The use of a basal infusion has also been recently shown to produce lower pain scores in the patients undergoing PCEA during labour[5,6].

After the initial induction, the success and effectiveness of epidural analgesia in this context could be dependent on a variety of factors, including the progress of labour[7] and the presence of dystocia[8]. As such, the need for individualisation of analgesic therapy cannot be overemphasised. It is also intuitive to suggest that while a basal infusion may not be imperative initially, it may be required as pain intensifies in the course of labour. For this pilot study, we have devised a programme, based on a novel clinical algorithm, that converts an ordinary continuous infusion pump into a PCEA pump that is responsive to the patient's needs. We called this computer-integrated PCEA (CI-PCEA). In CI-PCEA, the need for a basal infusion will be

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dependent on the history of the patient's analgesic requirement over the past hour. The magnitude of the basal infusion would be automatically and proportionally increased for a patient who makes more demands than one who does not.

The chief aim of our pilot study was to achieve seamless analgesia (defined here as one without breakthrough pain from induction of block to delivery) after the induction of combined spinal epidural analgesia (CSE) during early labour in 95% of the cases. This could potentially reduce the anaesthetist's workload and improve patients' satisfaction. If CI-PCEA could indeed reduce the incidence of breakthrough pain, the embedding of its algorithm into the currently-used continuous infusion pumps may be considered.

METHODS

This study was conducted with the approval of the Institutional Review Board, and informed written consent (including the liberty of withdrawing from the study at any point) was obtained from every patient who participated in the study. 40 healthy American Society of Anesthesiologists (ASA) 1 patients with cephalic presentation at ≥36 weeks of gestation and who were in early spontaneous labour (cervical dilatation ≤5 cm) and had requested neuraxial blocks for analgesia, were recruited. Patients who had received parenteral opioids in the last four hours and who had contraindications to neuraxial blocks (e.g. coagulopathy) were excluded. Patients who had multiple pregnancies, non-cephalic presentations, premature labour and obstetrial complications (e.g. pre-eclampsia, gestational mellitus and premature rupture of amniotic membranes) were also excluded.

After establishing an intravenous access, baseline systolic blood pressure and heart rate were measured noninvasively from the right brachial artery (Dinamap, Critikon, FL, USA). A baseline visual analogue pain score (VAPS based on a 0-10 scale; 0=no pain and 10=worst pain imagined) was also obtained. Only patients who had had a VAPS of >3 were recruited. After explaining the procedure to the patient, CSE was instituted by using the single space, needle through needle technique under aseptic conditions. All the blocks were performed by a single operator at the L3-4 interspace (by counting downwards from the C7 prominence) in the right lateral position. We used the loss of resistance to air technique to detect the epidural space with an 18 G Tuohy needle (Espocan, B.Braun, Melsungen, Germany). We injected less than 2 ml of air into the epidural space. The atraumatic 27G pencil point needle was then passed into the subarachnoid space and a free flow of cerebrospinal fluid was ensured before the standard dose of intrathecal analgesics, comprising 2 mg ropivacaine (Astra Zeneca, Sweden) and 15 μg of fentanyl (David Bull Laboratories, Melbourne, Australia) was injected over 15 seconds with orifice of the needle in the cephalad direction. The time of completion of injection was termed $Time_0$.

We then inserted the epidural catheter and kept 3-5 cm of it in the epidural space. Once there was no blood aspirated from the epidural catheter (signifying a low risk of intravascular catheterisation), it was flushed with 2 ml of 1.5% lidocaine (Xylocaine, Astrazeneca Laboratories, Sodertlaje, Sweden). The patients were then turned supine with 15% left lateral tilt. In the next minute after the block, the patient would be assigned, with the help of an opaque envelope containing a computer-generated number to receive one of the following regimens of 0.1% ropivacaine plus 2 μg/ml of fentanyl solution to maintain epidural analgesia:

1. Continuous epidural infusion (CEI, n=20) of 10 ml/h initiated 15 minutes after $Time_0$. This is the standard regimen utilised by anaesthetists in our institution; or
2. CI-PCEA (n=20) which was based on an empirical algorithm (Fig. 1).

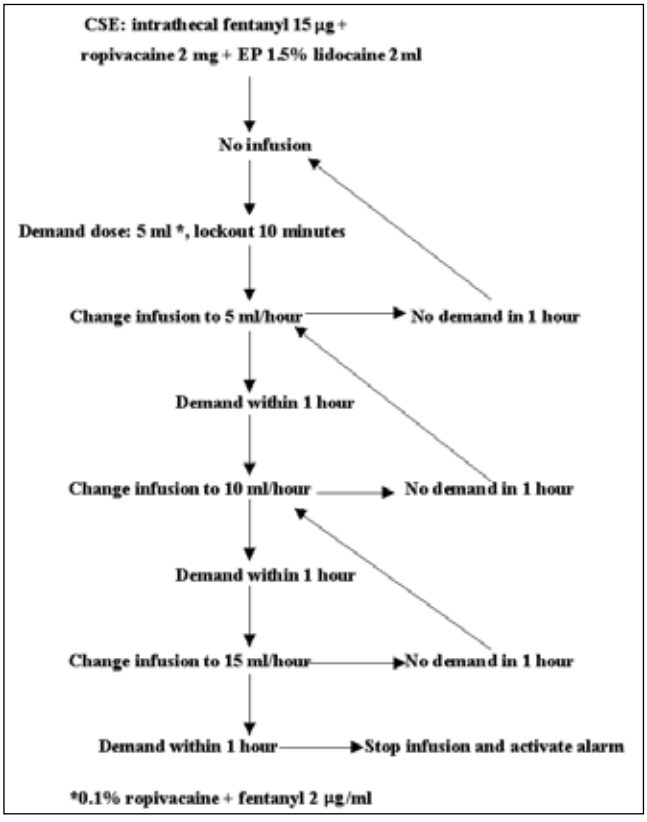


Fig. 1 Schematic representation of CI-PCEA algorithm

The assignment was done by another investigator who was not involved in performing the block or subsequent monitoring of the patients. In both regimens, the same infusion pump, IVAC P700 (Alaris, Basingstoke, UK) was used. When the patients were pain-free (VAPS <1) 15 minutes after CSE, they would be given a remote-controlled (wireless), modified hand-held computer "mouse". They were then instructed to self-administer an epidural bolus dose by clicking a button on this computer mouse. This served as the interface between the patient and the CI-PCEA/infusion pump, analogous to the PCEA "button" for the patient's self-administration of analgesics. They were counselled to self-bolus before pain reached an unbearable intensity, with the concept of lockout period clearly explained. The equal likelihood of receiving a "sham" PCEA was also explained, regardless of the group assigned.

The CI-PCEA programme source code was compiled in the Borland Pascal language on Windows Operating System. The reliability of the communications was performed by parity and cyclical redundancy checks based on the communication protocol provided by the service manual of the infusion pump. The two-way communications between the pump and the IBM Thinkpad laptop computer was accomplished by using their respective RS232 serial ports. The 5 ml boluses provided by CI-PCEA (which were time-cycled, based on an infusion rate of 150 ml/h) would take two minutes to complete (Fig. 2).

In our institution, the onset of a profound lower limb motor block (defined as the inability to flex either knee) and significant hypotension (defined as systolic blood pressure <90 mmHg or a reduction of systolic blood pressure of more than 25%) within the next ten minutes of $Time_0$ would behoove the investigation for a possible misplacement of the epidural catheter in the intrathecal space and exclude the patient from the study. Ambulatory epidural analgesia during labour is not routinely practised in our delivery suite. Failure to obtain cerebrospinal fluid after two attempts at dural puncture with the spinal needle would also exclude the patient from recruitment ("failed" block). In the event of an inadvertent intravascular or dural puncture by the epidural needle or catheter, the patient would be disqualified from recruitment into the study and managed according to the departmental protocols.

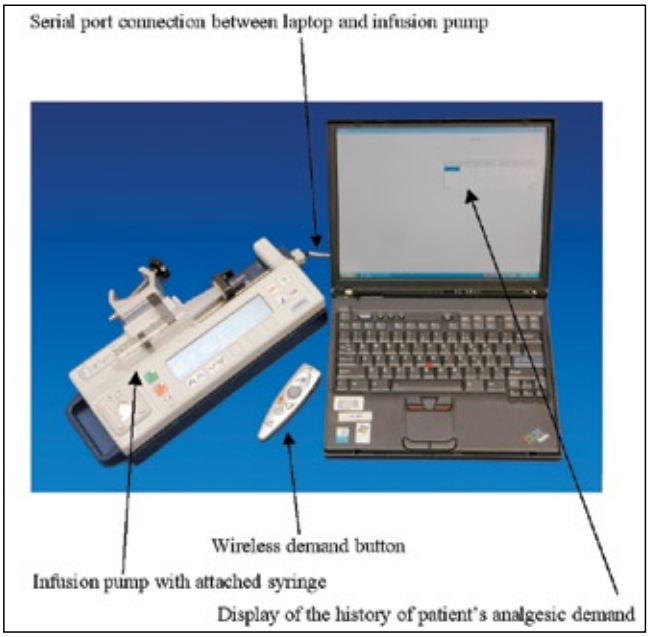


Fig. 2 Set-up of CI-PCEA.

The following parameters were monitored for the first half-hour after the block:

1. Systolic blood pressure and heart rate every five minutes.
2. Continuous foetal heart rate monitoring.
3. VAPS every ten minutes.
4. Lower limb motor block every ten minutes using the modified Bromage scale (0=no block; 1=unable to flex either hip joint but able to move knee and ankle joints; 2=unable to move hip and knee of either limb but able to move either ankle; 4=unable to move hip, knee or ankle joint of either lower limb).

If VAPS remained >1 at 15 minutes post-block and/or the patient complained of pain at that time, an incremental dose of epidural supplementation of 5 ml of 0.2% ropivacaine every ten minutes (up to a maximum of 15 ml) would be offered. This would be classified as an "ineffective" CSE and the patient would be removed from the study. The foetal heart monitoring would be done by a resident obstetrician who was not involved in the study. Abnormality of foetal heart tracing would be treated based on its cause, e.g. IV terbutaline 0.2 mg if uterine hyperstimulation was diagnosed.

For maintenance of analgesia, the following data were collected every two hours after $Time_0$ until delivery:

1. Systolic blood pressure and heart rate every five minutes.
2. Continuous foetal heart rate monitoring.
3. VAPS every ten minutes.
4. Sensory block at midline (loss of cold sensation to ice) every ten minutes.
5. Side effects: lower limb motor block every ten minutes using the modified Bromage scale (as above), shivering (0=no, 1=yes), significant hypotension, nausea (0=no, 1=yes), vomiting (0=no, 1=yes) and foetal bradycardia (0=no,

1=yes). The foetal heart rate was monitored continuously (via an external or scalp electrode) and reviewed by the resident obstetrician who was blinded to the regimen received by the patients.

At any time during the study, the patients were instructed to ask for immediate help from the anaesthetist if they felt that their pain was inadequately relieved, despite their epidural maintenance therapy. This event would be recorded as "breakthrough" pain – defined as the need for additional pain relief instituted by the anaesthetist despite CEI or CI-PCEA . The time when the patient experienced breakthrough pain ($Time_{end}$) would be recorded and the duration of analgesia ($Time_{painless}$) was taken mathematically as $Time_{end} - Time_0$. Pain scores, cervical dilatation and use of oxytocin at $Time_{end}$ were recorded. At $Time_{end}$, after ensuring that blood was not aspirated through the epidural catheter, the anaesthetist would institute an incremental dose of epidural supplementation of 5 ml of 0.2% ropivacaine every ten minutes (up to a maximum of 20 ml) followed by epidural fentanyl 50 μg until pain was relieved. A failure to achieve analgesia would render the catheter "ineffective" and the patient would also be removed from the study. Analgesia was continued until the delivery of the neonate.

When breakthrough pain occurred in the CI-PCEA group, a conversion to the default regimen, i.e. CEI would be effected while no change of regimen would be instituted to patients who were originally in the CEI group in this event. Patients in the CI-PCEA group would also be subjected to CEI once the maximum allowance for boluses plus infusion was reached, hence, resorting to the standard clinical practice of the institution in this event (Fig. 1). This would also potentially make any comparison of the purported drug-sparing effect of CI-PCEA with CEI more conservative and reduce the risk of type I error. Drug usage and the ratio of successful to total analgesic demand with CI-PCEA group was also documented every two hours as labour progressed. The time of delivery, mode of delivery, Apgar scores and overall satisfaction scores with labour analgesia (based on a 0-100 scale, 0=very dissatisfied, 100=extremely satisfied) were assessed and documented within two hours of delivery. The achievement of a "seamless" neuraxial analgesia, defined here as one without breakthrough pain from induction of block to delivery was recorded.

All data and statistical analyses were managed with the Statistical Package for Socieal Sciences (SPSS) version 9.0 (Chicago, IL, USA). The student's t test was used for the analysis of interval data which were normally distributed. Otherwise, the Mann-Whitney test was used. For nominal data and proportions, the χ^2 test with Yates correction when appropriate, was used. In the analysis of $Time_{end}$ (duration of analgesia), Kaplan-Maier analysis was used. As there was no actual $Time_{end}$ for subjects who had delivered before breakthrough pain occurred, the duration of time from $Time_0$ to the time of delivery of the neonates would be computed as the censored data of $Time_{painless}$ in the eventual Kaplan-Maier analysis. The sample size was determined (α=0.05, β=0.2) to detect a 45% difference in the incidence of "seamless" analgesia between CI-PCEA and CEI. The ability to achieve a 95% incidence of "seamless" analgesia in CI-PCEA was deemed clinically significant as this would potentially improve patients' satisfaction and reduce the anaesthetists' workload.

RESULTS

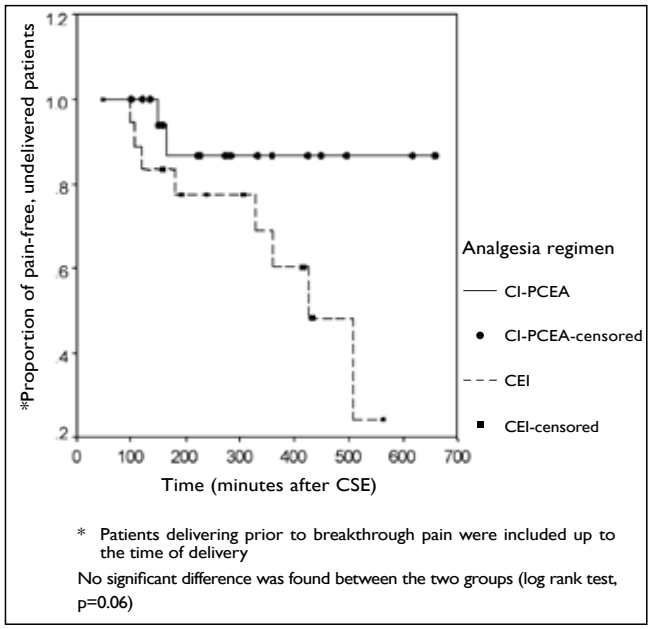
There were 20 patients recruited in each study group. There were no differences in patients' anthropometric and pre-analgesia data between the two groups (Table I). None of the patients had an "ineffective" block. There was a significant difference in the incidence of breakthrough pain, i.e. the primary outcome measure (two in CI-PCEA versus eight in the CEI group, p=0.027). There was a trend towards a longer mean $Time_{painless}$ for CI-PCEA (591 min, 95% confidence interval [CI] 504-679 versus 399 minutes, 95% CI 315-481 for CEI, p=0.06 from log rank test) with Kaplan-Maier analysis (Fig. 3). There were also no differences in the characteristics of labour analgesia, side effects and obstetrical outcome

Table 1. Patients' anthropometric and pre-analgesia data.

	CEI (n=20)	CI-PCEA (n=20)
Height (cm)	159 ± 6	160 ± 6
Weight (kg)	72 ± 11	66 ± 10
Preblock cervical dilatation (cm)	3 (2-5)	3 (2-5)
Preblock use of oxytocin	6	5
Preblock systolic blood pressure (mmHg)	115 ± 12	115 ± 11
Preblock heart rate (beats/min)	75 ± 10	80 ± 14
Preblock pain scores (0-10 VAS)	8 (7-10)	8 (5-10)

Values are expressed as mean ± SD or median (minimum – maximum), except for the preblock use of oxytocin where absolute numbers of patients are expressed.

No statistically significant differences were found between the groups.



* Patients delivering prior to breakthrough pain were included up to the time of delivery

No significant difference was found between the two groups (log rank test, p=0.06)

Fig. 3 Proportion of CI-PCEA and CEI patients without breakthrough pain versus time after intrathecal injection.

Table II. Characteristics of labor analgesia, side effects and obstetric outcome.

	CEI	CI-PCEA
Maximum dermatomal block to cold	T6 (T10-T3)	T4 (T10-T1)
Pain score (VAPS) >1 during maintenance of analgesia	4	7
Lower limb motor block (Bromage score >0)	3	1
Lowest systolic blood pressure (mmHg)	108 (101-127)	108 (98-124)
Pain score (VAPS) at $Time_{end}$	7 (3-10)	8 (7-9)
Cervical dilatation (cm) at $Time_{end}$	5 (3-10)	4.5 (3-6)
Use of oxytocin at $Time_{end}$	5	2
Pruritus	9	11
Nausea + vomiting	2	2
Duration of labour (min)	314 (101-659)	283 (69-760)
Duration of second stage (min)	116 (40-175)	64 (15-179)
Mode of delivery		
Normal	12	3
Vaginal instrumental	5	15
Caesarean section	1	2
Foetal birthweight (kg)	3.1 (2.3-3.9)	3.2 (2.6-3.8)
Apgar score >7 at five minutes post-birth	17	19
Patient's satisfaction with analgesia (0-100 VAS)	95 (80-100)	97 (80-100)

Values were expressed as median (minimum – maximum) or absolute numbers of patients.

No statistically significant difference was found between the two groups.

between the two regimens (Table II). None of the patients had significant hypotension during the study. There was no reported foetal bradycardia within 30 minutes of $Time_0$ that had required uterine relaxation or caesarean section. There was no difference in the total hourly consumption of epidural ropivacaine (infusion + boluses) between the two groups (median=12.2 mg/h, maximum=13.6 mg, minimum=9.8 mg for CEI versus 10.0 mg/h, 17.1 mg/h, 4.6 mg/h, respectively, for CI-PCEA, p=0.166). The median proportion of successful to total patient analgesic demands for CI-PCEA was 0.83 (minimum=0.5 to maximum=1). Based on the data of the total hourly consumption of epidural ropivacaine of CEI (mean 10.8, SD 3), post-hoc analysis showed that our study was adequately powered (α=0.05, β=0.2) to detect a 25% difference between the two groups in this respect.

DISCUSSION

Our study showed that the use of CI-PCEA reduced the incidence of breakthrough pain. As a corollary, the need for anaesthetists' intervention in providing supplemental analgesia would be potentially reduced. A delay in providing rescue analgesia in our busy labour and delivery floor could also potentially undermine the quality of labour analgesia. Despite the small sample size, Kaplan-Maier analysis also suggested a trend towards a longer duration of analgesia ($Time_{painless}$) in the CI-PCEA group. Even though we were unable to demonstrate a difference in the hourly consumption of local anaesthetics between the two groups during the maintenance phase of epidural analgesia, we could infer that CI-PCEA did improve the customisation of analgesia in accordance with patients' needs as far as reducing the incidence of the first breakthrough pain.

However, we could not demonstrate a difference in patients' satisfaction between CI-PCEA and CEI as our study was underpowered in this regard. Moreover, the conditions of our study were not reflective of real life as the patients in CEI were given a sham PCEA button which could have rendered a positive psychological impact of seemingly affording some autonomy in determining the degree of desired analgesia. In addition, all patients were closely monitored and frequently reviewed by the caregivers. This could have enhanced the overall analgesic experience, hence, making any difference in the quality of analgesia between the two regimens difficult to distinguish.

Indeed, our preliminary results suggested that CI-PCEA could provide another alternative to maintaining labour epidural analgesia by allowing the patients

the flexibility of receiving pain relief on demand on top of a basal infusion that is also responsive to their analgesic needs in the previous hour. The literature is currently still unclear with regard to the role of a basal infusion[3,5,6]. While some authors suggested that a basal infusion in conjunction with PCEA would increase drug consumption without an apparent analgesic benefit[2], others have purported that the addition of a basal infusion could reduce the need for analgesic supplementation[4]. In a recent review of PCEA for labour analgesia, a basal infusion has been proposed to reduce the anesthestists' workload while PCEA devoid of a basal infusion has been suggested as a strategy to reduce analgesic consumption[9]. In fact, the need for a basal infusion is also probably influenced by other clinical factors, such as, the progress of labour[7,8] and the incidence of dystocia[10].

As the frequency of demands over the last hour is reflective of the increasing intensity of pain, the incremental infusion rates of the current CI-PCEA regimen is designed, in principle, to tailor the magnitude of a continuous basal infusion to be commensurate with the degree of pain experienced. With the current CI-PCEA regimen, we had hoped to "close the loop" by according a higher infusion rate to those who had needed it, as reflected by the frequency of analgesic demands over the previous hour. In this respect, CI-PCEA, which conserves the local anaesthetic used initially but progressively increases its basal infusion with increased pain due to progress of labour, appears to be intuitive.

The bolus volume of 5 ml was chosen because a previous study had demonstrated that regardless of concentration, this minimal volume was desirable to ensure an appropriate spread of block[11]. Indeed, our study had demonstrated the superiority of CI-PCEA in terms of reducing breakthrough pain. This could also be attributed to an improved spread of analgesics in the epidural space when boluses of PCEA were given instead of CEI[12]. The primary aim of this preliminary study was to establish the feasibility of CI-PCEA in comparison with CEI (our standard institutional practice). With the current results, further research on the clinical role of the "wandering" infusion rate as well as the usefulness of CI-PCEA in comparison with conventional PCEA (with or without a basal infusion), is warranted.

In this preliminary study, we did not observe any adverse clinical side effects in the two groups, given the small sample size. The CI-PCEA programme was tested in vitro by the investigators independently, before the initiation of the clinical trial. Throughout the study, we did not encounter any problem with regard to the connections of the equipment, as all the cables were securely attached by screws and locks. In this cohort of patients, fidelity to the CI-PCEA protocol was reproduced in every case. The built-in alarm when further analgesic demands are made despite a maximal basal infusion, set arbitrarily at 15 ml/h is a safety mechanism which would trigger the need for a closer assessment of the patient for situations such as a dislodge of the epidural catheter or a patchy block.

In conclusion, our study showed that CI-PCEA could replace CEI as the mode of maintenance for epidural analgesia. CI-PCEA reduced the incidence of breakthrough pain without the evidence of increasing drug consumption. Our study also showed that with the CI-PCEA programme, we were able to convert an ordinary infusion pump to one that analyses the patients' needs in the previous hour (based on analgesic demands) and automatically adjusts the basal infusion accordingly. More research is required to define and refine the clinical role of CI-PCEA for labour analgesia.

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